

REMARKS

The present amendment restores originally submitted claims 10-17 and adds new claims 18-39 for examination at this time. The submission of this amendment is to pursue certain embodiments of the invention not pursued in the parent applications. Applicant reserves the right to file additional continuation applications to further prosecute various embodiments previously pursued in the parent applications.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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MWR:sj

Enclosures:

Postcard
Sequence Listing on Paper
Sequence Listing on Diskette

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend the specification by inserting the enclosed "SEQUENCE LISTING" immediately preceding the claims.

Please replace the Title with the following rewritten Title:

METHOD OF MAKING GLYCOPROTEIN EXHIBITING ERYTHROPOIESIS
REGULATING ACTIVITY AND GLYCOPROTEIN PRODUCED BY THIS METHOD
 [HUMAN ERYTHROPOIETIN GENE: HIGH LEVEL EXPRESSION IN STABLY
 TRANSFECTED MAMMALIAN CELLS]

Please replace the paragraph beginning at page 2, line 16, with the following rewritten paragraph:

FIGURE 1 is a schematic representation of the subject 2426 bp Apa I restriction fragment that contains the human erythropoietin gene sequences (SEQ ID NO:1).

Please replace the paragraph beginning at page 3, line 13, with the following rewritten paragraph:

Oligonucleotide mixtures were prepared using an Applied Biosystems synthesizer and end-labeled using ³²p-ATP and T4 polynucleotide kinase. The synthetic oligonucleotides were designed to correspond to portions of the amino terminal amino acid sequence (SEQ ID NO:2) of:

H₂N-Ala-Pro-?-Arg-Leu-Ile-Leu-Asp-Ser-Arg-Val-Leu-Glu-Arg-Tyr-Leu-Leu-
 Glu-Ala-Lys-Glu-Ala-Glu-?-Ile-Thr-Asp-Gly-Gly-Ala

obtained by Yanagawa et al. (J.Biol.Chem. 259:2707-2710,1984) for the human protein purified from urine of patients with aplastic anemia. To reduce the degeneracy of the codons for the amino acid sequence of this region, the codon usage rules of Grantham et al. (Nucleic Acids Research 8:43-59, 1981) and Jaye et al. (Nucleic Acids Research 11:2325-2335, 1983) were employed. These rules take into account the relatively rare occurrence of CpG dinucleotides in DNA of vertebrates and avoid, where appropriate, potential A:G mismatch pairings. At amino acid position 24, an asparagine was placed as most likely (J.Biol.Chem. 259:2707-2710,1984). For the amino acids Glu-Ala-Lys-Glu-Ala-Glu-Asn (SEQ ID NO:3), 2 pools of 72 sequences each were synthesized to correspond to the predicted codons. Thus, one pool was TT(c/t)TC(a/g/t)GC(c/t)TC(c/t)TT(a/g/t)GCTTC (SEQ ID NO:4) for the 20 nucleotide probe, and the second pool replaced a T with a C at position 18. For the amino acids Glu-Asn-Ile-Thr-Asp-Gly (SEQ ID NO:5), one pool of sequences (AGC TCC TCC ATC AGT ATT ATT T[c/t]) (SEQ ID NO:6) was constructed for the 23 nucleotide probe.

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